Abstract

Introduction: Diabetes is a widespread chronic disease. Repaglinide was approved by the FDA in 1998 as an oral hypoglycemic drug. Repaglinide has a good anti-diabetic effect, but it suffers from a number of problems, including low bioavailability, poor water solubility and extensive first-pass hepatic metabolism. Our aim in this study was to use solid lipid nanoparticles (SLN) with chitosan coating to improve oral administration of repaglinide. Oral administration of SLNs can reduce first-pass hepatic metabolism and increase the oral bioavailability of the drug. Compared to other carriers, SLN nanoparticles offer several advantages such as good tolerability, biodegradability and the possibility of large-scale industrial production. Also, the addition of chitosan to the surface of nanoparticles due to its adhesive property increases the penetration ability of the drug-loaded lipid carriers from mucosal surfaces.

Method: Optimization of nanoparticles investigation of the effect of various parameters on their particle size was performed using Design Expert software. Using the dilution method, a calibration diagram was drawn and finally the equation of this diagram was used to determine the amount of drug in unknown samples. The properties of the nanoparticles were evaluated using various techniques such as dynamic light scattering, thermal analysis, Fourier transform infrared spectroscopy (FTIR) and scanning electron microscopy. Also, the rate of drug entrapment and drug loading efficiency were calculated. The drug release profile was evaluated using the dialysis bag method and the concentration of the released drug was determined by ultraviolet-visible spectroscopy. The in vivo study oral administration of the drug-loaded nanocarriers was evaluated on a number of rats and the blood glucose in plasma was measured at specific times.

Results, discussion and conclusions: The size of SLN nanoparticles in optimum formulation (76.5 nm) was within the acceptable range for SLN nanoparticles. According to the results, increasing the concentration of stearic acid and chitosan increases the size of nanoparticles and increasing the concentration of tween 80 and glycerol monostearate reduces the size of nanoparticles. Drug entrapment and drug loading were calculated to be 90% and 11%, respectively. The results of FTIR and thermal analysis showed no chemical interaction between the carrier and the drug. Also, according to the results of FTIR, the presence of amide bonds between stearic acid and chitosan confirmed the structure and formation of final nanocarriers. The results of scanning electron microscope showed the spherical structure of the nanoparticles. The drug release profile in nanoparticles with chitosan coating is slower than nanoparticles without chitosan coating. The results of in vivo study and oral administration of the drug to rat showed that repaglinide-loaded nanoparticles reduced blood sugar more than pure repaglinide. Also, nanoparticles with chitosan coating showed better performance than nanoparticles without coating.

Keywords: Solid lipid nanoparticles, Repaglinide, Diabetes, Chitosan, oral drug delivery, Bioavailability